

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

Claim 1. (Currently Amended) A synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes a mammalian human heparanase protein, the sequence of nucleotides comprising two consensus cleavage sites recognized by an endoproteinase, wherein the cleavage sites are selected from the group consisting of: tobacco etch virus (TEV) protease cleavage sites, 3C protease cleavage sites from picornavirus, thrombin protease cleavage sites, enterokinase cleavage sites and factor Xa cleavage sites, and wherein the cleavage sites are located between nucleotides encoding residues 100 and 168 of the heparanase protein.

Claim 2. (Original) A vector comprising the nucleic acid molecule of claim 1.

Claim 3. (Canceled)

Claim 4. (Currently Amended) An isolated A host cell comprising the vector of claim 2 3.

Claim 5. (Currently Amended) The isolated host cell of claim 4, wherein the host cell is an insect cell or a yeast cell.

Claim 6. (Canceled)

Claim 7. (Currently Amended) The isolated host cell of claim 5, wherein the host cell is a yeast cell which is selected from the group consisting of: *Pichia pastoris*, *Hansenula polymorpha* and *Saccharomyces cervisiae*.

Claim 8. (Canceled)

Claim 9. (Currently Amended) The synthetic nucleic acid molecule of claim 18, wherein the consensus cleavage sites are located before residues G110 and K158 of the human heparanase protein.

Claim 10. (Canceled)

Claim 11. (Currently Amended) A synthetic mammalian human heparanase nucleic acid molecule comprising a portion that encodes a mammalian human heparanase protein, the protein coding portion consisting essentially of a sequence of nucleotides encoding an N-terminal fragment of about 8 kDa and comprising a sequence of amino acids as set forth in SEQ ID NO:15, a linker, and a sequence of nucleotides encoding a C-terminal fragment of about 50 kDa and comprising a sequence of amino acids as set forth in SEQ ID NO:16, wherein the N-terminal and C-terminal fragments encode protein fragments that are substantially similar to wild-type human heparanase fragments, and wherein the encoded human heparanase protein is constitutively active.

Claim 12. (Canceled)

Claim 13. (Previously Presented) The synthetic nucleic acid molecule of claim 11, wherein the linker comprises a sequence of nucleotides that encodes a central loop region of the hyaluronidase protein.

Claim 14. (Previously Presented) The synthetic nucleic acid molecule of claim 13, wherein the hyaluronidase is from *H. manillensis*.

Claim 15. (Currently Amended) The synthetic nucleic acid molecule of claim 11 12, wherein the linker comprises a sequence of nucleotides that encodes a (GlySer)₃ linker.

Claim 16. (Currently Amended) A vector comprising the synthetic nucleic acid molecule of claim 11 12.

Claim 17. (Currently Amended) An isolated A host cell comprising the vector of claim 16.

Claim 18. (Currently Amended) The isolated host cell of claim 17 which is an insect cell or a yeast cell.

Claim 19. (Canceled)

Claim 20. (Currently Amended) A method of expressing mammalian human heparanase in non-mammalian cells comprising:

- (a) transforming or transfecting non-mammalian cells with a vector comprising a sequence of nucleotides that encodes a mammalian human heparanase protein, the sequence of nucleotides comprising two heterologous consensus cleavage sites recognized by an endoproteinase, , wherein the cleavage sites are selected from the group consisting of: tobacco etch virus (TEV) protease cleavage sites, 3C protease cleavage sites from picornavirus, thrombin protease cleavage sites, enterokinase cleavage sites and factor Xa cleavage sites, and wherein the cleavage sites are located between residues 100 and 168 of the human heparanase protein;
- (b) culturing the host cell under conditions which allow expression of said human heparanase protein;
- (c) disrupting the cells and at least partially purifying the human heparanase protein; and
- (d) exposing the at least partially purified human heparanase protein to the endoproteinase, wherein the heparanase protein is cleaved at the consensus cleavage sites by the endoproteinase.

Claim 21. (Canceled)

Claim 22. (Currently Amended) A method of expressing a single chain, constitutively active mammalian human heparanase in non-mammalian cells comprising:

- (a) transforming or transfecting non-mammalian cells with a vector comprising a synthetic mammalian human heparanase gene, wherein the synthetic gene comprises a portion that encodes the human heparanase protein, the protein coding portion consisting essentially of a sequence of nucleotides encoding an N-terminal fragment of about 8 kDa, the N-terminal fragment comprising a sequence of amino acids as set forth in SEQ ID NO:15, a sequence of nucleotides encoding a linker and a sequence of nucleotides encoding a C-terminal fragment of about 50 kDa, the C-terminal fragment comprising a sequence of amino acids as set forth in SEQ ID NO:16, wherein the N-terminal and C-terminal fragments encode protein fragments that are substantially similar to wild type fragments; and
- (b) culturing the host cell under conditions which allow expression of said human heparanase protein; wherein the human heparanase protein is constitutively active.

Claim 23. (Canceled)

US Appln. No.: 10/572,796
US Filing Date: 3/21/2006
Case No.: ITR0060YP
Page No.: 5

Claim 24. (Original) The method of claim 22 wherein the linker comprises a central (GlySer)₃.

Claim 25. (Canceled)